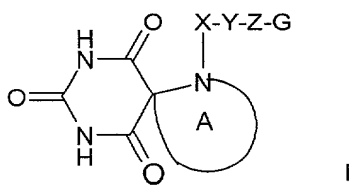
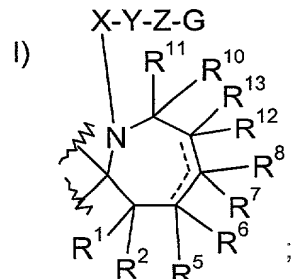
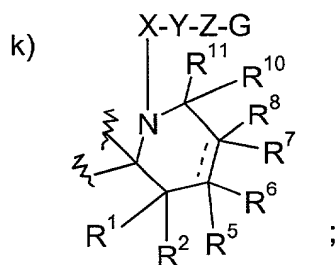
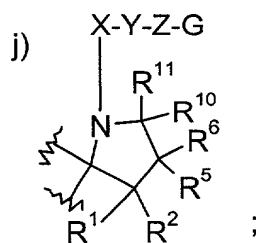
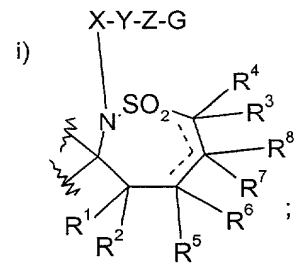
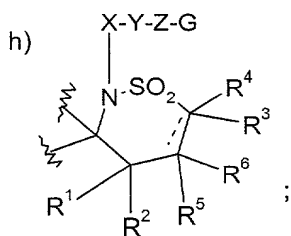
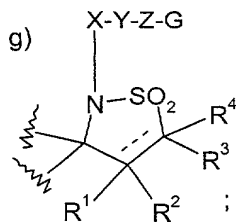
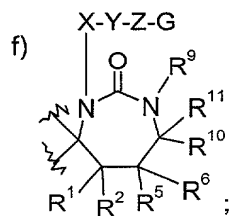
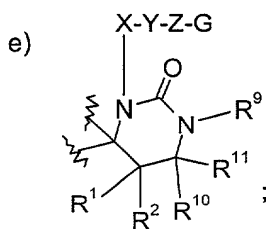
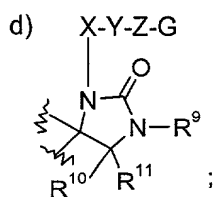
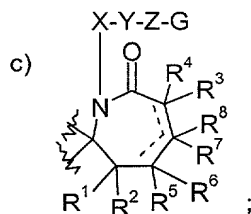
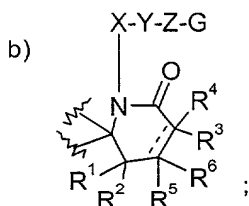
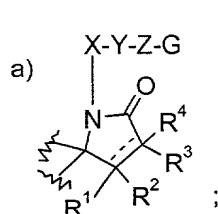


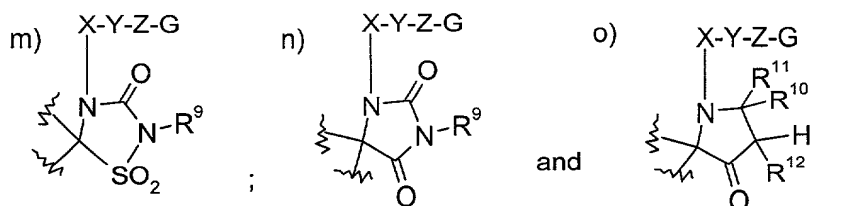
We Claim:

1. A compound of the formula:



wherein said "A" is a 5-7 membered heterocyclic ring selected from the group consisting of:





wherein each of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , R^{11} , R^{12} and R^{13} is independently selected from the group consisting of hydrogen, (C₁-C₄)alkyl, (C₁-C₄)alkenyl, (C₁-C₄)alkynyl, (C₆-C₁₀)aryl, (C₁-C₁₀)heteroaryl, (C₃-C₈)cycloalkyl and (C₁-C₁₀)heterocyclyl; wherein each of said (C₁-C₄)alkyl, (C₆-C₁₀)aryl, (C₁-C₁₀)heteroaryl, (C₃-C₈)cycloalkyl and (C₁-C₁₀)heterocyclyl may be optionally substituted on any of the ring carbon atoms capable of forming an additional bond with 1-3 substituents per ring independently selected from halo, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, -CN, -OH and -NH₂;

X is (C₆-C₁₀)aryl or (C₁-C₁₀)heteroaryl;

Y is selected from the group consisting of a bond, oxygen, sulfur, >C=O, >SO₂, >S=O, -CH₂-, -CH₂O-, -O(CH₂)_n-, -CH₂S-, -S(CH₂)_n-, -CH₂SO-, -CH₂SO₂-, -SO(CH₂)_n-, -SO₂(CH₂)_n-, -NR¹⁴, -NR¹⁴(CH₂)_n-, -CH₂[N(R¹⁴)]-, -CH₂(CH₂)_n-, -CH=CH-, -C≡C-, -[N(R¹⁴)]-SO₂- and -SO₂[N(R¹⁴)]-;

n is an integer from one to four;

R¹⁴ is hydrogen or (C₁-C₄)alkyl;

Z is selected from the group consisting of (C₆-C₁₀)aryl, (C₃-C₈)cycloalkyl, (C₁-C₁₀)heterocyclyl and (C₁-C₁₀)heteroaryl; wherein one or two carbon-carbon single bonds of said (C₃-C₈)cycloalkyl or (C₁-C₁₀)heterocyclyl may optionally be replaced by carbon-carbon double bonds;

wherein each of said X or Z may be independently optionally substituted on any of the ring carbon atoms capable of forming an additional bond by one or two substituents per ring independently selected from F, Cl, Br, CN, OH, (C₁-C₄)alkyl, (C₁-C₄)perfluoroalkyl, (C₁-C₄)perfluoroalkoxy, (C₁-C₄)alkoxy and (C₃-C₈)cycloalkyloxy;

G is R¹⁵-(CR¹⁶R¹⁷)_p-; wherein G is a substituent on any ring carbon atom of Z capable of forming an additional bond and is oriented at a position other than alpha to the point of attachment of the Z ring to Y;

p is an integer from 0 to 4;

R¹⁵ is independently selected from the group consisting of halo, -CN, -NO₂, OH, (C₁-C₄)alkenyl, (C₁-C₄)alkynyl, (C₁-C₄)perfluoroalkyl, perfluoro(C₁-C₄)alkoxy, R¹⁸-, R¹⁸-O-, R¹⁸-(C₁-C₄)alkyl-O-, R¹⁸-(C=O)-, R¹⁸-(C=O)-O-, R¹⁸-O-(C=O)-, R¹⁸-S-, R²²-(S=O)-, R¹⁸-(SO₂)-, R²²-(SO₂)-(NR²¹)-, R¹⁹-(C=O)-(NR²¹)-, R²²-O-(C=O)-(NR²¹)-, (R¹⁹R²⁰)N-, (R¹⁹R²⁰)N-(SO₂)-, (R¹⁹R²⁰)N-(C=O)-; (R¹⁹R²⁰)N-(C=O)-(NR²¹)- and (R¹⁹R²⁰)N-(C=O)-O-;

each of R¹⁶ and R¹⁷ are independently selected from hydrogen and (C₁-C₄)alkyl;

or R¹⁶ and R¹⁷ may optionally be taken together with the carbon to which they are attached to form a 5 to 10-membered carbocyclic ring;

R¹⁸, R¹⁹, R²⁰ and R²¹ are independently selected from the group consisting of hydrogen, (C₁-C₄)alkyl, (C₆-C₁₀)aryl, (C₃-C₈)cycloalkyl, (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl; wherein said (C₆-C₁₀)aryl, (C₃-C₈)cycloalkyl, (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl moieties may be optionally substituted on any of the ring carbon atoms capable of forming an additional bond by one to three substituents per ring independently selected from F, Cl, Br, CN, OH, (C₁-C₄)alkyl, (C₁-C₄)perfluoroalkyl, (C₁-C₄)perfluoroalkoxy, (C₁-C₄)alkoxy, amino, (C₁-C₄)alkyl-NH-, [(C₁-C₄)alkyl]₂-N- and (C₃-C₈)cycloalkyloxy; wherein said (C₃-C₈)cycloalkyl and (C₁-C₁₀)heterocyclyl moieties may also optionally be substituted by oxo; wherein said (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl moieties may optionally be substituted on any ring nitrogen atom able to support an additional substituent by one to two substituents per ring independently selected from the group consisting of (C₁-C₄)alkyl and (C₁-C₄)alkyl-(C=O)-;

or R¹⁹ and R²⁰ may optionally be taken together with the nitrogen to which they are attached to form a 3 to 8-membered heterocyclic ring;

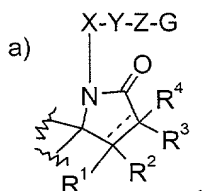
or R¹⁹ and R²¹ may optionally be taken together with the nitrogen, the carbon or the oxygen to which they are attached to form a 3 to 8-membered heterocyclic ring;

R²² is selected from the group consisting of (C₁-C₄)alkyl, (C₆-C₁₀)aryl, (C₃-C₈)cycloalkyl, (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl; wherein said (C₆-C₁₀)aryl, (C₃-C₈)cycloalkyl, (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl moieties may be optionally substituted on any of the ring carbon atoms capable of forming an additional bond by one to three substituents per ring independently selected from F, Cl, Br, CN, OH, (C₁-C₄)alkyl, (C₁-C₄)perfluoroalkyl, (C₁-C₄)perfluoroalkoxy, (C₁-C₄)alkoxy, amino, (C₁-C₄)alkyl-NH-, [(C₁-C₄)alkyl]₂-N- and (C₃-C₈)cycloalkyloxy; wherein said (C₃-C₈)cycloalkyl and (C₁-C₁₀)heterocyclyl moieties may also optionally be substituted by oxo; wherein said (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl moieties may optionally be substituted on any ring nitrogen atom able to support an additional substituent by one to two substituents per ring independently selected from the group consisting of (C₁-C₄)alkyl and (C₁-C₄)alkyl-(C=O)-;

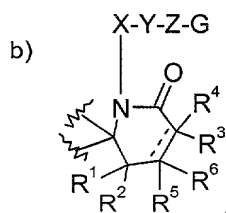
or R²¹ and R²² may optionally be taken together with the nitrogen, the oxygen or the sulfur to which they are attached to form a 3 to 8-membered heterocyclic ring;

or a pharmaceutically acceptable salt thereof.

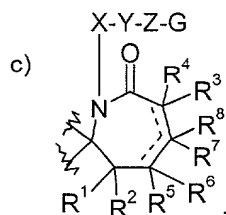
2. The compound according to claim 1 wherein said "A" is



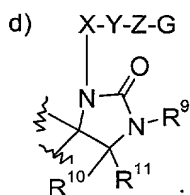
3. The compound according to claim 1 wherein said "A" is



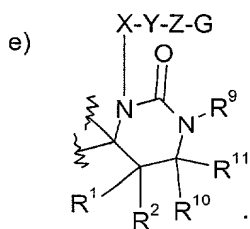
4. The compound according to claim 1 wherein said "A" is



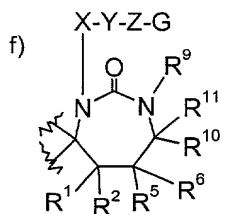
5. The compound according to claim 1 wherein said "A" is



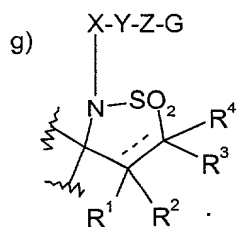
6. The compound according to claim 1 wherein said "A" is



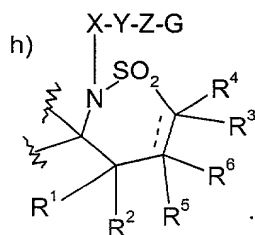
7. The compound according to claim 1 wherein said "A" is



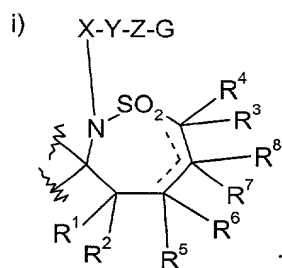
8. The compound according to claim 1 wherein said "A" is



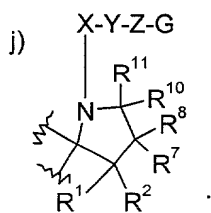
9. The compound according to claim 1 wherein said "A" is



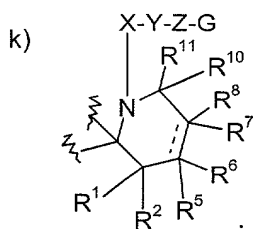
10. The compound according to claim 1 wherein said "A" is



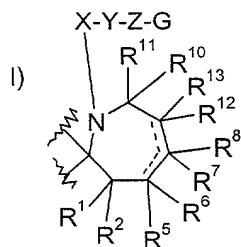
11. The compound according to claim 1 wherein said "A" is



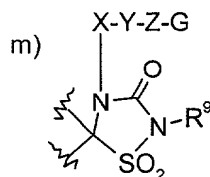
12. The compound according to claim 1 wherein said "A" is



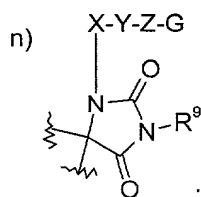
13. The compound according to claim 1 wherein said "A" is



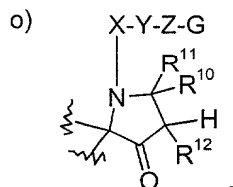
14. The compound according to claim 1 wherein said "A" is



15. The compound according to claim 1 wherein said "A" is



16. The compound according to claim 1 wherein said "A" is



17. The compound according to claim 1 wherein said X is (C₆-C₁₀)aryl.

18. The compound according to claim 1 wherein said X is phenyl.

19. The compound according to claim 1 wherein said X is (C₁-C₁₀)heteroaryl.

20. The compound according to claim 19 wherein said (C₁-C₁₀)heteroaryl is

selected from the group consisting of benzimidazolyl, benzofuranyl, benzofurazanyl, 2H-1-benzopyranyl, benzothiadiazine, benzothiazinyl, benzothiazolyl, benzothiophenyl, benzoxazolyl, chromanyl, cinnoliny, furazanyl, furopyridinyl, furyl, imidazolyl, indazolyl, indolinyl, indoliziny, indolyl, 3H-indolyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, phthalazinyl, pteridinyl, purinyl, pyrazinyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrazolyl, pyrrolyl, quinazoliny, quinolinyl, quinoxaliny, tetrazolyl, thiazolyl, thiadiazolyl, thienyl, triazinyl and triazolyl, wherein said (C₁-C₁₀)heteroaryl is optionally substituted on any of the ring carbon atoms capable of forming an additional bond by one or

two substituents per ring independently selected from F, Cl, Br, CN, OH, (C₁-C₄)alkyl, (C₁-C₄)perfluoroalkyl, (C₁-C₄)perfluoroalkoxy, (C₁-C₄)alkoxy and (C₃-C₈)cycloalkyloxy.

21. The compound according to claim 19 wherein said (C₁-C₁₀)heteroaryl is selected from the group consisting of imidazolyl, isothiazolyl, isoxazolyl, oxadiazolyl, oxazolyl, pyrazinyl, pyridazinyl, pyridinyl, pyrimidinyl and pyrazolyl.

22. The compound according to claim 19 wherein said (C₁-C₁₀)heteroaryl is selected from the group consisting of pyrazinyl, pyridazinyl, pyridyl and pyrimidinyl.

23. The compound according to claim 1 wherein said Y is selected from the group consisting of a bond, oxygen, >C=O, -CH₂-, -CH₂O-, -O(CH₂)_n-, -CH₂CH₂-, -CH=CH- and -C≡C-; wherein n is 1 or 2.

24. The compound according to claim 23 wherein said Y is oxygen.

25. The compound according to claim 1 wherein said Y is selected from the group consisting of sulfur, >SO₂, >S=O, -CH₂S-, -S(CH₂)_n-, -CH₂SO-, -CH₂SO₂-, -SOCH₂- and -SO₂(CH₂)_n-; wherein n is 1 or 2.

26. The compound according to claim 1 wherein said Y is selected from the group consisting of -CH₂[N(R¹⁴)]-, >NR¹⁴-, -NR¹⁴(CH₂)_n-, -SO₂[N(R¹⁴)]- and -[N(R¹⁴)]-SO₂-.

27. The compound according to claim 1 wherein said Z is selected from the group consisting of (C₆-C₁₀)aryl or (C₁-C₁₀)heteroaryl; wherein said Z may be optionally substituted on any of the ring carbon atoms capable of forming an additional bond by one or two substituents per ring independently selected from F, Cl, Br, CN, OH, (C₁-C₄)alkyl, (C₁-C₄)perfluoroalkyl, (C₁-C₄)perfluoroalkoxy, (C₁-C₄)alkoxy and (C₃-C₈)cycloalkyloxy.

28. The compound according to claim 1 wherein said Z is (C₆-C₁₀)aryl; wherein said Z is substituted on any of the ring carbon atoms capable of forming an additional bond by one or two substituents per ring independently selected from F, Cl, CN, (C₁-C₄)alkyl, (C₁-C₄)perfluoroalkyl and (C₁-C₄)alkoxy.

29. The compound according to claim 1 wherein said G is R¹⁵-(CR¹⁶R¹⁷)_p; wherein p is 0.

30. The compound according to claim 29 wherein said R¹⁵ is selected from the group consisting of halo, -CN and R¹⁸; wherein R¹⁸ is selected from the group consisting of hydrogen, (C₁-C₄)alkyl, (C₆-C₁₀)aryl, (C₃-C₈)cycloalkyl, (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl; wherein said (C₆-C₁₀)aryl, (C₃-C₈)cycloalkyl, (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl moieties may be optionally substituted on any of the ring carbon atoms capable of forming an additional bond by one to three substituents per ring independently selected from F, Cl, Br, CN, OH, (C₁-C₄)alkyl, (C₁-C₄)perfluoroalkyl, (C₁-C₄)perfluoroalkoxy, (C₁-C₄)alkoxy, amino, (C₁-C₄)alkyl-NH-, [(C₁-C₄)alkyl]₂-N- and (C₃-C₈)cycloalkyloxy; wherein said (C₃-C₈)cycloalkyl and (C₁-C₁₀)heterocyclyl moieties may also optionally be substituted by oxo; wherein said (C₁-C₁₀)heteroaryl and (C₁-C₁₀)heterocyclyl moieties may optionally be

substituted on any ring nitrogen atom able to support an additional substituent by one to two substituents per ring independently selected from the group consisting of (C₁-C₄)alkyl and (C₁-C₄)alkyl-(C=O)-.

31. The compound according to claim 29, wherein said R¹⁵ is selected from the group consisting of hydrogen, -CN, halo and oxadiazolyl.

32. The compound according to claim 29, wherein said G is oriented at a position *meta* to the point of attachment of the Z ring to Y.

33. The compound according to claim 29, wherein said G is oriented at a position *para* to the point of attachment of the Z ring to Y.

34. The compound according to claim 1 wherein said G is R¹⁵-(CR¹⁶R¹⁷)_p; wherein p is an integer from 1 to 4.

35. The compound according to claim 34, wherein R¹⁵ is selected from the group consisting of (C₁-C₁₀)heteroaryl; R¹⁹-(C=O)-(NR²¹)-, (R¹⁹R²⁰)N-, (R¹⁹R²⁰)N-(C=O)-(NR²¹)- and R²²-O-(C=O)-(NR²¹);

each of R¹⁶ and R¹⁷ are independently hydrogen or (C₁-C₄)alkyl;

R¹⁹ is (C₁-C₄)alkyl or (C₃-C₈)cycloalkyl;

R²⁰ is hydrogen or (C₁-C₁₀)heteroaryl selected from the group consisting of 2-oxazolyl, 2-pyrazolyl and 3-pyrazolyl;

R²¹ is hydrogen or (C₁-C₄)alkyl; and

R²² is (C₁-C₄)alkyl or (C₃-C₈)cycloalkyl.

36. The compound according to claim 34, wherein R¹⁵ is 2-pyrazolyl; and each of R¹⁶ and R¹⁷ are independently hydrogen.

37. The compound according to claim 34, wherein R¹⁵ has the formula R¹⁹-(C=O)-(NR²¹)-; each of R¹⁶ and R¹⁷ are independently hydrogen or (C₁-C₄)alkyl; R¹⁹ is selected from the group consisting of methyl, ethyl, propyl, butyl and cyclobutyl; and R²¹ is hydrogen.

38. The compound according to claim 34, wherein R¹⁵ is selected from the group consisting of (R¹⁹R²⁰)N-, (R¹⁹R²⁰)N-(SO₂)-, (R¹⁹R²⁰)N-(C=O)-; (R¹⁹R²⁰)N-(C=O)-(NR²¹)- and (R¹⁹R²⁰)N-(C=O)-O-; wherein R¹⁹ and R²⁰ are taken together with the nitrogen to which they are attached to form a 3 to 8-membered heterocyclic ring.

39. The compound according to claim 34, wherein R¹⁵ is selected from the group consisting of R¹⁹-(C=O)-NR²¹-; R²²-(SO₂)-NR²¹-; R²²-O-(C=O)-(NR²¹) and (R¹⁹R²⁰)N-(C=O)-NR²¹-;

each of R¹⁶ and R¹⁷ are independently hydrogen or (C₁-C₄)alkyl;

R¹⁹ and R²¹ are taken together with the nitrogen, the carbon or the oxygen to which they are attached to form a 3-8 membered heterocyclic ring; and

R²¹ and R²² are taken together with the nitrogen, the carbon or the oxygen to which they are attached to form a 3-8 membered heterocyclic ring.

40. The compound according to claim 34, wherein G is oriented at a position *meta* to the point of attachment of the Z ring to Y.

41. The compound according to claim 34, wherein G is oriented at a position *para* to the point of attachment of the Z ring to Y.

5 42. The compound according to claim 1, wherein said compound is selected from the group consisting of:

1-[6-(4-Fluoro-phenoxy)-pyridin-3-yl]-1,7,9-triaza-spiro[4.5]decane-2,6,8,10-tetraone;

1-[6-(4-Fluoro-phenoxy)-pyridin-3-yl]-1,8,10-triaza-spiro[5.5]undecane-2,7,9,11-tetraone;

10 4-[5-(2,6,8,10-Tetraoxo-1,7,9-triaza-spiro[4.5]dec-1-yl)-pyridin-2-yloxy]-benzonitrile;

1-[6-(4-[1,3,4]oxadiazol-2-yl-phenoxy)-pyridin-3-yl]-1,7,9-triaza-spiro[4.5]decane-2,6,8,10-tetraone;

1-[6-(4-Ethyl-phenoxy)-pyridin-3-yl]-1,7,9-triaza-spiro[4.5]decane-2,6,8,10-tetraone;

15 N-[4-[5-(2,6,8,10-Tetraoxo-1,7,9-triaza-spiro[4.5]dec-1-yl)-pyridin-2-yloxy]-benzyl]-acetamide;

N-[4-[5-(2,6,8,10-Tetraoxo-1,7,9-triaza-spiro[4.5]dec-1-yl)-pyridin-2-yloxy]-benzyl]-propionamide;

N-[4-[5-(2,6,8,10-Tetraoxo-1,7,9-triaza-spiro[4.5]dec-1-yl)-pyridin-2-yloxy]-benzyl]-butyramide;

20 Pentanoic acid 4-[5-(2,6,8,10-tetraoxo-1,7,9-triaza-spiro[4.5]dec-1-yl)-pyridin-2-yloxy]-benzylamide;

Cyclobutanecarboxylic acid 4-[5-(2,6,8,10-tetraoxo-1,7,9-triaza-spiro[4.5]dec-1-yl)-pyridin-2-yloxy]-benzylamide;

1-[6-(4-Bromo-phenoxy)-pyridin-3-yl]-1,7,9-triaza-spiro[4.5]decane-2,6,8,10-tetraone;

25 1-[6-(4-pyrazol-1-ylmethyl-phenoxy)-pyridin-3-yl]-1,7,9-triaza-spiro[4.5]decane-2,6,8,10-tetraone;

and a pharmaceutically acceptable salt thereof.

43. A pharmaceutical composition for the treatment of a condition selected from the group consisting of connective tissue disorders, inflammatory disorders, immunology/allergy disorders, infectious diseases, respiratory diseases, cardiovascular diseases, eye diseases, metabolic diseases, central nervous system disorders, liver/kidney diseases, reproductive health disorders, gastric disorders, skin disorders and cancers in a mammal, including a human, comprising an amount of a compound of claim 1 effective in such treatment and a pharmaceutically acceptable carrier.

35 44. A method for treating a condition selected from the group consisting of connective tissue disorders, inflammatory disorders, immunology/allergy disorders, infectious diseases, respiratory diseases, cardiovascular diseases, eye diseases, metabolic diseases, central nervous system disorders, liver/kidney diseases, reproductive health disorders, gastric

disorders, skin disorders and cancers in a mammal, including a human, comprising administering to said mammal an amount of a compound of claim 1, effective in treating such a condition.

- 5 45. A pharmaceutical composition for the treatment of a condition which can be treated by the inhibition of matrix metalloproteinases in a mammal, including a human, comprising an amount of a compound of claim 1 effective in such treatment and a pharmaceutically acceptable carrier.